

What is claimed is:

1 1. A device for manipulating a molecule *in vivo* relative to a target tissue
2 comprising a support and at least one electrode member extending away from and affixed
3 to or defining the support, the at least one electrode member having a plurality of
4 conductive portions and a nonconductive portion, wherein:

5 the conductive portions are positioned in spaced-apart relation from each
6 other, each conductive portion being in circuit communication with a respective portion of
7 a source of electrical energy;

8 the conductive portions are configured to establish a first electromagnetic
9 field between selected conductive portions sufficient to manipulate a molecule relative to
10 a target tissue and a second electromagnetic field sufficient to cause transient permeability
11 of a cell membrane within the target tissue; and

12 at least two of the conductive portions are locatable against a selected
13 portion of the target tissue.

1 2. The device recited in Claim 1, wherein the conductive portions and the
2 nonconductive portion are located on a single support member.

1 3. The device recited in Claim 1, wherein the conductive portions and
2 nonconductive portion are located on separate support members.

1 4. The device recited in Claim 1, wherein the electrode member comprises a
2 plurality of electrode members affixed to the support and the conductive portions and the
3 nonconductive portions are located along the electrode members.

1 5. The device recited in Claim 1, wherein the conductive and the nonconductive
2 portions comprise even pairs thereof.

1 6. The device recited in Claim 1, wherein the conductive and the nonconductive
2 portions comprise uneven pairs thereof.

1 7. The device recited in Claim 1, wherein the support comprises a generally
2 cylindrical post having a portal therethrough from a top end to a bottom end and the device
3 further comprises:

4 a disc affixed to the post bottom end, the disc having a bottom surface having
5 an outer downwardly depending annulus comprising alternating sectors of conductive and
6 nonconductive areas, the electrode member comprising the annulus and the conductive
7 portions comprising the conductive sectors; and

8 a lead in circuit communication with each conductive area and extending from
9 the disc through the post portal to the top end thereof.

1 8. The device recited in Claim 7, wherein the disc has a noncircular shape.

1 **9.** The device recited in Claim 7, further comprising:
2 a plurality of contact means positioned adjacent the post portal top end and
3 in circuit communication with each lead; and
4 interface means positioned adjacent the post portal top end having means
5 for communicating with each contact means for establishing circuit communication with a
6 signal generator.

1 **10.** The device recited in Claim 9, wherein:
2 each of the contact means comprises a contact brush affixed within the portal
3 against an inner wall thereof; and
4 the interface means comprises a key interlock insertable within the portal at
5 the top end thereof and having a contact pad positioned for communication with each
6 contact brush.

1 **11.** The device recited in Claim 7, wherein the disc comprises a flexible material
2 for permitting shape adaptation with the selected portion of the target tissue.

1 **12.** The device recited in Claim 7, wherein the disc comprises a portion having
2 sufficient transparency to permit visualization of the target tissue selected portion
3 therethrough.

1 **13.** The device recited in Claim 1, further comprising means for delivering a
2 preselected pattern of signals to selected pairs of the conductive portions to effect a
3 desired molecular result.

1 **14.** The device recited in Claim 13, wherein the conductive and nonconductive
2 portions comprise even pairs thereof.

1 **15.** The device recited in Claim 13, wherein the conductive and nonconductive
2 portions comprise uneven pairs thereof.

1 **16.** The device recited in Claim 1, further comprising a downwardly depending
2 post affixed adjacent a bottom end of the support, the post having at least one conductive
3 area on a surface thereof.

1 **17.** The device recited in Claim 16, wherein the downwardly depending post has
2 a plurality of conductive portions thereon.

1 **18.** The device recited in Claim 17, wherein the conductive and the
2 nonconductive portions comprise even pairs thereof.

1 **19.** The device recited in Claim 17, wherein the conductive and the
2 nonconductive portions comprise uneven pairs thereof.

1 **20.** The device recited in Claim 16, wherein the downwardly depending post has
2 a single conductive portion thereon comprising an electrode.

1 **21.** The device recited in Claim 20, wherein the post comprises a plurality of
2 downwardly depending posts, each post axially movable between a first position and a
3 second position lower than the first position and biased to the second position, for
4 achieving contact between each post and a target tissue surface.

1 **22.** The device recited in Claim 21, wherein each post is affixed to the support
2 in spring-loaded fashion.

1 **23.** The device recited in Claim 21, wherein each post extends in a generally
2 linear fashion from the distal end of the support.

1 **24.** The device recited in Claim 21, wherein the posts are curved with respect to
2 the distal end of the support.

1 **25.** The device recited in Claim 16, wherein each post has a pointed conductive
2 bottom tip, the tips disposed at a radially inwardly facing angle to each other, each post
3 inwardly movable between a first position and a second position wherein the tips are closer
4 together than in the first position, the second position for gripping tissue between the tips.

1 **26.** The device recited in Claim 1, further comprising a pair of electrode-bearing
2 members movably affixed to the support in separation-adjustable fashion, each electrode-
3 bearing member comprising means for affixing at least one electrode thereto.

1 **27.** The device recited in Claim 26, wherein each electrode-bearing member
2 comprises an insulating plate, and wherein the electrode members comprise a plurality of
3 electrodes affixed to an inward-facing surface of each plate, the plates configured to grip
4 at least a portion of the target tissue therebetween.

1 **28.** The device recited in Claim 1, further comprising means for establishing at
2 least one pair of opposite-polarity voltages approximately simultaneously on a respective
3 pair of conductive portions.

1 **29.** The device recited in Claim 1, further comprising means for selectively
2 activating each conductive portion in a predetermined pattern.

1 **30.** The device recited in Claim 29, wherein the source of electrical energy
2 comprises a signal generator and the activating means comprises software means in
3 controlling relation to the signal generator.

1 **31.** The device recited in Claim 1, wherein the support has a lumen therethrough
2 dimensioned for admitting a syringe needle thereinto to permit an introduction of a
3 substance containing the molecule into the target tissue.

1 **32.** The device recited in Claim 1, further comprising a needle member
2 depending from a bottom of the support, the needle member having a pointed tip and an
3 opening adjacent the tip, the tip and the opening positioned beneath the electrode
4 member, the needle member adapted to deliver a substance containing the molecule
5 through the opening into the target tissue.

1 **33.** The device recited in Claim 1, further comprising means for facilitating
2 attachment of the electrode member to the target tissue.

1 **34.** The device recited in Claim 33, wherein the facilitating means comprises a
2 mechanical means.

1 **35.** The device recited in Claim 33, wherein the facilitating means is selected
2 from a group consisting of a barb and surface roughness.

1 **36.** The device recited in Claim 33, wherein the facilitating means comprises a
2 chemical means.

1 **37.** The device recited in Claim 36, wherein the facilitating means is selected
2 from a group consisting of bioadhesives and adhesives.

1 **38.** A method for achieving a desired distribution and delivery of a molecule from
2 an initial location into a target tissue, the method comprising the steps of:

3 placing at least one electrode-bearing member containing areas of
4 conductivity capable of having reverse polarities, generally adjacent, but in nonpenetrating
5 fashion to, a surface adjacent a target tissue, each electrode in circuit communication with
6 a respective portion of a source of electrical energy;

7 establishing a first electrical potential between a pair of the areas of
8 conductivity sufficient to cause electromigration of the desired molecule from the initial
9 location toward the target tissue; and

10 establishing a second electrical potential between a pair of areas of
11 conductivity higher than the first electrical potential sufficient to cause electroporation in
12 the target tissue for enhancing a movement of the desired molecule into a cell thereof.

1 **39.** The method recited in Claim 38, wherein the establishing steps comprise
2 establishing a series of first and second electrical potentials in a predetermined sequence
3 of pulses.

1 **40.** The method recited in Claim 38, further comprising the step of establishing
2 a third electrical potential between a pair of areas of conductivity sufficient to cause

electromigration of the desired molecule from a location adjacent the target tissue through a pore in a cell membrane of the target tissue into an interior thereof.

41. The method recited in Claim 40, wherein the establishing steps comprise establishing a series of first, second, and third electrical potentials in a predetermined sequence of pulses.

42. The method recited in Claim 38, wherein the electrode members are configured to at least partially surround a surface projection or a projection within an orifice near a periphery of the target tissue.

43. The method recited in Claim 38, wherein the electromigration is effected to cause the molecule to be delivered beneath a skin layer.

44. A method for delivering a bioactive molecule from an initial location to a target tissue, the method comprising the steps of:

placing at least one electrode member having areas of conductivity of opposite polarities against a surface generally adjacent, but in nonpenetrating fashion to, a target tissue, each member bearing sections of reverse polarity, each electrode member being in circuit communication with a respective portion of a source of electrical energy;

7 activating a pair of the areas of opposite polarity to achieve an
8 electromigration of the bioactive molecule from the initial location to a location adjacent the
9 target tissue; and

10 activating a pair of the areas of conductivity to achieve electroporation of a
11 cell membrane within the target tissue sufficient to permit entry of the biological molecule
12 into the cell interior.

1 **45.** The method recited in Claim 44, wherein the electromigration is effected to
2 cause the molecule to penetrate a skin layer.

1 **46.** A method for bringing two molecules from two respective initial locations into
2 apposition at a desired target tissue site for permitting a reaction therebetween, the method
3 comprising the steps of:

4 placing an electrode member containing at least two areas of conductivity
5 thereon against a surface adjacent a desired target tissue site;

6 activating the areas of conductivity to cause an electromigration of the first
7 and the second molecule to a third area adjacent the target tissue site; and

8 permitting the first and the second molecule to react at the third area.

1 **47.** The method recited in Claim 46, wherein the activating step comprises
2 establishing an electrical potential between the pairs of areas of conductivity sufficient to
3 cause the electromigration of the first and second molecule in a desired direction.

1 **48.** The method recited in Claim 47, wherein the electromigration is effected to
2 cause the first and the second molecule to penetrate a skin layer.

1 **49.** The method recited in Claims 46, wherein the activation step causes the first
2 and the second molecule to be delivered to an internal compartment or cytosol of cells
3 comprising the target tissue.

1 **50.** The method recited in Claim 46, wherein the penetration step is effected
2 through a biological tissue other than skin.

1 **51.** The method recited in Claims 46, wherein the activating step is sufficient to
2 cause electromigration but is insufficient to cause electroporation.

1 **52.** The method recited in Claim 46, further comprising the step, prior to the
2 activating step, of activating the areas of conductivity to cause an electroporation of the
3 target tissue.

1 **53.** The method recited in Claim 46, wherein the electromigration is effected from
2 a plurality of sides of the target tissue, and wherein the electrode member comprises a
3 plurality of electrode members adjacent the target tissue.

1 **54.** The method recited in Claim 53, wherein the electrode member comprises
2 a plurality of electrode members, and wherein the activating step is sufficient to effect
3 electromigration but is insufficient to effect electroporation.

1 **55.** The method recited in Claims 46, further comprising the step, following the
2 activating step, of activating the areas of conductivity sufficiently to cause electroporation
3 in the target tissue.

1 **56.** The method recited in Claims 46, further comprising the step, substantially
2 simultaneously with the activating step, of activating the areas of conductivity sufficient to
3 cause electroporation in the target tissue.

1 **57.** A method for making a molecule electromanipulator comprising the steps of:
2 affixing at least one member containing areas of discrete conductivity to a
3 support in spaced-apart relation, each area of conductivity being differentially activatable;
4 providing circuit communication between each conductivity area and a source
5 of electrical energy, the conductive areas configured to establish a low-level
6 electromagnetic field *in vivo* between selected conductivity areas for manipulating a
7 molecule relative to a target tissue and a higher-level electromagnetic field for causing
8 transient permeability of a cell membrane within the target tissue; and

9 providing switching means between each conductivity area and the electrical
10 energy source to permit differential activation of the areas of differing conductivity on each
11 electrode member.

1 **58.** The method recited in Claim 57, further comprising the step of providing
2 means for controlling the switching means adapted to activate the areas of conductivity in
3 a preselected pattern.